UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

July 27, 2022

MEMORANDUM:

Subject:	Name of Pesticide Product:	GF-5040
	EPA Reg. No. /File Symbol:	62719-TAA
	DP Barcode:	DP 464770
	Decision No.:	580826
	Action Code:	(R314)
	Submission:	#1079754
	E-Sub.	#70827
	PC Codes:	121601 (Acetochlor: 30%)
		123009 (Topramezone: 0.5%)
		117403 (Clopyralid: 2.67%)

From: Byron T. Backus, Ph.D., Biologist
CITAB
Registration Division (7505T)

To: Aleah Holt / Emily Schmid, RM 25
Herbicide Branch
Registration Division (7505T)

Registrant: CORTEVA AGRISCIENCE LLC

FORMULATION FROM PROPOSED LABEL:

		by wt.
121601	Acetochlor: 2-chloro-N-ethoxymethyl-N-(2-ethyl-6-methylphenyl)acetamide	30.0%
123009	Topramezone: [3-(4,5-dihydro-3-isoxazolyl)-2-methyl-4-(methylsulfonyl) phenyl](5-hydroxy-1H-pyrazol-4-yl) methanone	0.5%
117403	Clopyralid MEA salt: 3,6-dichloropyridinecarboxylic acid, Monoethanolamine salt	2.67%
Other Ingredients		66.83%
Total		100.0%

Contains 333 grams/liter or 2.78 pounds/gallon acetochlor, 5.55 grams/liter or 0.046 pounds/gallon topramezone, and 29.59 grams/liter or 0.247 pounds/gallon clopyralid, acid equivalent (3,6-dichloropyridinecarboxylic acid)

ACTION REQUESTED: "The registrant has submitted a new end use product, a first combination of AIs for registration (R314) using a selective to satisfy acute tox requirements. New MRIDs (51661403-08) have been submitted. Please review the following materials to conduct a review and determine acute tox categories/precautionary text: Application form, Cover letter, data matrix (12/16/2021), proposed Basic CSF (dated 12/13/2021) and proposed label can be found in Documentum under Submission #1079754…"

BACKGROUND: The material available for review includes a Transmittal Document (dated December 16, 2021) stating that this is an application for a new Section 3 product registration and "GF-5040 is a new encapsulated herbicide for postemergence control of annual grasses and broadleaf weeds in field corn, field seed corn, field silage corn and popcorn." The form 8570-1 (December 16, 2021) states that this is a Section 3 application for new registration. The data matrix (December 16, 2021) cites (p. 1) the following MRIDs to address the acute toxicity data requirements: 51661403 (870.1100), 51661404 (870.1200), 51661405 (870.1300), 51661406 (870.2400), 51661407 (870.2500) and 51661408 (a waiver request for 870.2600); these MRIDs have been submitted for review as part of the application package. The proposed label for 62719-TAA has the signal words CAUTION/PRECAUCION and precautionary statements indicating it is in toxicity category III for oral and dermal toxicity (although the first aid statements in the order in which they are presented are If in Eyes, If on Skin or Clothing and If Swallowed). In addition, the proposed precautionary statements indicate ("Prolonged or Frequently Repeated Skin Contact May Cause Allergic Reactions in Some Individuals") that this formulation is a dermal sensitizer. There is a proposed Basic CSF (dated 13-Dec-21) for 62719-TAA in Documentum with the Agency notation "Inerts Approved for Food Use under 40 CFR 180.920, Pre-Harvest Application to Growing Crops."

COMMENTS AND RECOMMENDATIONS:

1. The five acute toxicity studies in MRIDs 516614-03 through -07 have been reviewed and classified as acceptable (refer to the attached DER).

2. The dermal sensitization study waiver request in MRID 51661408 includes (p. 5) the following: "Corteva is proposing that an acute skin sensitization study for GF-5040 can be waived based on available results from acetochlor and a similar formulation as well as a calculation method. As similar formulations with acetochlor have shown skin sensitization, in order to avoid additional testing on animals, Corteva proposes that GF-5040 be classified as a skin sensitizer." This study is waived with the stipulation that this product be classified and labeled as a dermal sensitizer.

3. Based on the results from MRIDs 516614-03 through -07 and the waiver request in MRID 51661408 with classification as a positive dermal sensitizer, the following is the acute toxicity profile for 62719-TAA:

acute oral toxicity	III	Acceptable	MRID 51661403
acute dermal toxicity	III	Acceptable	MRID 51661404
acute inhalation toxicity	IV	Acceptable	MRID 51661405
primary eye irritation	IV	Acceptable	MRID 51661406
primary skin irritation	IV	Acceptable	MRID 51661407
dermal sensitization	positive	Waived	MRID 51661408*

*Waiver request.

4. Based on the acute toxicity profile given above, the proposed uses and information from the CSF, the following are the precautionary and first aid statements for 62719-TAA as obtained from the Label Review System:

Product ID: 62719-TAA
Product Name: GF-5040

Precautionary Statements:

Keep out of Reach of Children.
Signal Word: CAUTION

The registrant has included the Spanish signal word PRECAUCION and the statement: "Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.) These are appropriate and acceptable.

Poison Label: None
Hazards to Humans and Domestic Animals:

Harmful if swallowed. Harmful if absorbed through skin.

Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Wear long-sleeved shirt and long pants, socks, shoes, and waterproof gloves. Remove and wash contaminated clothing before reuse. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

Additional labeling should include (but not necessarily be limited to) the following:
Follow the manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

User Safety Recommendations

Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.
Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing

First Aid:

If swallowed:
- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to do so by a poison control center or doctor.
- Do not give anything by mouth to an unconscious person.

If on skin or clothing:
- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.

The registrant has proposed an If in eyes first aid statement. This is acceptable, however, this statement (addressing a toxicity category IV hazard) should follow the If swallowed and If on skin or clothing statements (addressing toxicity category III hazards).

EPA encourages, but does not require (see PR Notice 2001-1) registrants to include a company telephone number or toll-free hotline for emergency information in the first aid section. If a number is included, confusion can be avoided by specifying emergency vs non-emergency numbers. It should include a phrase or statement indicating the kinds of information the number should be used for and it may include hours of service. The following are examples of appropriate statements that may be included on the label:

- Have the product container or label with you when calling a poison control center or doctor or going for treatment.
- For medical emergencies, call the poison control center at 1-800-222-1222.
- For general information about this product, call 1-XXX-XXX-XXXX [may include hours of service], or contact the National Pesticides Information Center (NPIC) at 1-800-858-7378, Monday through Friday, 8 AM to 12 PM PST, or at http://npic.orst.edu.

5. All acute toxicity data requirements for the registration of 62719-TAA have been satisfied by MRIDs 516614-03 through -07 and waiver of the data sensitization study requirement (870.2600) with classification and labeling as a positive dermal sensitizer.

6. The If in eyes statement first aid statement (addressing a toxicity category IV hazard) should follow the If swallowed and If on skin or clothing statements (addressing toxicity category III hazards). The remainder of the precautionary and first aid labeling statements are acceptable.

7. The Basic CSF (dated 13 Dec. 2021) for 62719-TAA and any chemistry data or references to chemistry data should also be reviewed and accepted by the product chemists in the Chemistry, Inerts and Toxicology Assessment Branch.

DATA EVALUATION RECORD

GF-5040

STUDY TYPES: ACUTE ORAL TOXICITY - RAT [OCSPP 870.1100; OECD 423]
ACUTE DERMAL TOXICITY - RAT [OCSPP 870.1200; OECD 402]
ACUTE INHALATION TOXICITY - RAT [OCSPP 870.1300; OECD 436]
ACUTE EYE IRRITATION - RABBIT [OCSPP 870.2400; OECD 405]
ACUTE DERMAL IRRITATION - RABBIT [OCSPP 870.2500; OECD 404]

MRIDs 51661403, 51661404, 51661405, 51661406, and 51661407

Prepared for
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Task Order No. AcuteTox-4-217

Primary Reviewer:
Jennifer Goldberg, B.S.

Signature: Jennifer Goldberg
Date: 06/17/2022

Secondary Reviewers:
Susan S. Little, Ph.D., DABT (2016-2021)

Signature: Susan S. Little
Date: 06/17/2022

Robert H. Ross, M.S., Project Manager

Signature: Robert H. Ross
Date: 06/17/2022

Quality Assurance:
Angela M. Edmonds, B.S.

Signature: Angela M. Edmonds
Date: 06/17/2022

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

DATA EVALUATION RECORD

Reviewers: Byron T. Backus, Ph.D. (EPA) **Date:** July 27, 2022
Jennifer Goldberg, B.S. (Summitec Corp.)

Product Reg. No./File Symbol: 62719-TAA

1. DP BARCODE: 464770				
2. PC CODE(S): 117403, 121601, 123009				
3. CURRENT DATE: July 27, 2022				
4. TEST MATERIAL: GF-5040: 3.3% Clopyralid-olamine (36.1 g/L) (CAS # not provided), 0.5% Topramezone (5.39 g/L) (CAS # not provided), 30.7% Acetochlor (334 g/L) (CAS # not provided); Batch No. ENBK-176110-008; JRF Test Item Code: ACT268; light tan/off-white liquid; pH 5.47 (1% aqueous solution in distilled water) (per JRF); density 1.0874 g/mL at 20°C; re-certification date: July 7, 2023; stored at room temperature.				
Study/Species/Lab Study #/Date	**MRID**	**Results**	**Tox Cat**	**Core Grade ***
Acute oral toxicity/ Wistar rat (Acute Toxic Class Method) Jai Research Foundation (Gujarat, India) Study No. 401-1-01-28615 November 20, 2021 OCSPP 870.1100; OECD 423	51661403	**LD_{50} > 2000 mg/kg bw** 6 fasted female rats were administered 2000 mg/kg bw undiluted test substance. All animals survived, gained body weight during both study weeks, and appeared normal for the duration of the study. No gross abnormalities were observed at necropsy.	**III**	**A**
Acute dermal toxicity/ Wistar rat Jai Research Foundation (Gujarat, India) Study No. 403-1-01-28616 November 15, 2021 OCSPP 870.1200; OECD 402	51661404	**LD_{50} > 2000 mg/kg bw** 3 female rats were dermally exposed for 24 hours to 2000 mg/kg bw of the test substance as received. All animals survived and appeared normal for the duration of the study. All animals gained body weight during both study weeks. No dermal effects were seen, and no gross abnormalities were found at necropsy.	**III**	**A**

		Study deficiencies: • Some dose sites were likely less than 10% of total body surface. • Rats were 14-15 weeks of age instead of 8-12 weeks.		
Acute inhalation toxicity/Sprague Dawley rat (4-hour, Nose-only) (Acute Toxic Class Method) Haskell R&D Center (Newark, Delaware) Study No. 22528-721 November 29, 2021 OCSPP 870.1300; OECD 436	51661405	**LC_{50} > 5.1 mg/L (both sexes)** 6 rats (3/sex) were exposed to the test substance diluted 1:1 (v/v) with distilled water aerosolized at 5.1 mg/L. Mean gravimetric chamber conc.: 5.1 mg/L; Average MMAD: 3.0 μm; Average GSD: 2.25; Nominal conc.: 822 mg/L. All animals survived and gained body weight overall. One female lost body weight during Days 1-2 and Days 8-10, then gained weight in between and thereafter. Other than wet facial fur on Day 1 in all animals and facial hair loss in one female on Days 2-3, all animals appeared normal for the duration of the study. No gross abnormalities were observed at necropsy. Study deficiencies: • Exposure chamber relative humidity (100%) was above the recommended range of 30-70%. • Samples for MMAD determination were collected only twice during exposure rather than the 3-4 times specified in OCSPP 870.1300 for studies that do not have 2 MMAD measurements taken during	**IV**	**A**

		a pre-test trial that are within 10% of each other.		
Primary eye irritation/ New Zealand White rabbit Jai Research Foundation (Gujarat, India) Study No. 407-1-01-28618 November 20, 2021 OCSPP 870.2400; OECD 405	51661406	**Mildly irritating** **MMTS = 4.0 at 1 hour** The test substance (0.1 mL) as received was instilled into the right eye of three female young adult rabbits. Each eye was anesthetized with proparacaine HCl, and systemic analgesia was provided. No corneal opacity, iritis, or discharge was seen during the study. At 1 hour post dose, all treated eyes exhibited conjunctival redness (grade = 1) and chemosis (grade = 1). All eyes were free of chemosis by 24 hours and conjunctival redness by 72 hours. No positive fluorescein staining occurred. All animals appeared otherwise normal for the duration of the study and gained body weight.	**IV**	**A**
Primary dermal irritation/New Zealand White rabbit Jai Research Foundation (Gujarat, India) Study No. 406-1-01-28617 November 19, 2021 OCSPP 870.2500; OECD 404	51661407	**Slightly Irritating;** **Mean irritation at 72 hrs = 0.0** **PDII = 0.5** Three male rabbits were exposed for 4 hours to 0.5 mL of the test substance as received. At 1 hour after patch removal, very slight erythema (score = 1) and very slight edema (score = 1) was observed on all dose sites. All sites were free of dermal irritation by 24 hours. All animals appeared otherwise normal for the duration of the study and gained body weight.	**IV**	**A**

Dermal sensitization/ OCSPP 870.2600	51661408 (waiver request)	**Waived with classification as a positive dermal sensitizer.** From p. 5 of MRID 51661408: "Corteva is proposing that an acute skin sensitization study for GF-5040 can be waived based on available results from acetochlor and a similar formulation as well as a calculation method. As similar formulations with acetochlor have shown skin sensitization, in order to avoid additional testing on animals, Corteva proposes that GF-5040 be classified as a skin sensitizer." This study is waived with the stipulation that this product be classified and labeled as a dermal sensitizer.	--	**W**

***Core Grade Key: A =Acceptable; S = Supplementary; U = Unacceptable; D = Data Gap; W = W**